GLYCOLIPID & SPHINGOLIPID RESEARCH JUNE 2020

New Deuterium-labeled Glycosphingolipids

High-purity deuterated glycosphingolipids are ideal for the identification and quantification of gangliosides in samples and biological systems using mass spectrometry techniques. While a variety of D_3 -labeled glycosphingolipids have long been available in our catalog, we have synthesized a new set of D_9 -labeled gangliosides and a globotriaosylceramide that enable improved separation of the labeled m/z from the naturally occurring material and its abundant isotopes. With a better means for separation, this improves the quantitation of these compounds in biological samples by LC-MS/MS methods.

For example, consider the natural isotopic abundance of GM_1 in the top of the figure below compared to the D_3 -labeled (middle spectrum) and D_9 -labeled (bottom spectrum) versions.



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ATRFYA I I C

Lipids and Biochemicals A Cayman Chemical Company

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m/z

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1528.90

1529.91

1531.91

1533.92

1535.92

1537.93

Because this compound has a large molecular weight with multiple carbon atoms, the ¹³C abundance is quite high up to the M+5 isotope. Indeed, the M+3 isotope (1519.85 m/z) is very significant at 14.4%. This is the portion of natural GM₁ that contains three ¹³C atoms, and it has approximately the same mass as GM₁-D₃, which is 1519.86 m/z. This natural M+3 isotope can contribute to variability in the isotopically labeled internal standard response as GM₁ levels vary from sample to sample and can negatively impact quantification of GM₁. A standard labeled with nine deuterium atoms overcomes this problem because the natural abundance of GM₁ with nine ¹³C atoms is effectively zero. That is, the natural isotopes will not interfere with the GM₁-D_a signal.



N-omega-CD₃- Octadecanoyl monosialoganglioside GM₁ (NH₄ + salt) Catalog No. 2050



N-Hexadecanoyl-D $_9}\,(13,13,14,14,15,15,16,16,16)-monosialoganglioside <math display="inline">{\rm GM}_1\,({\rm NH}_4\,^+\,{\rm salt})$ Catalog No. 2057

Available D₉-Labeled Glycosphingolipids

Catalog No.	Product Name	Formula Weight	Purity
2057	N-Hexadecanoyl-D $_{9}$ (13,13,14,14,15,15,16,16,16)-monosialoganglioside $GM_{1}(NH_{4}^{+}\operatorname{salt})$	1528 + NH ₃	98+%
2058	$N\text{-}Hexadecanoyl-D_{9}(13,13,14,14,15,15,16,16,16)\text{-}monosialogangliosideGM_{2}(NH_{4}^{+}salt)$	1366 + NH ₃	98+%
2059	$N\text{-}Hexadecanoyl-D_{9}(13,13,14,14,15,15,16,16,16)\text{-}monosialogangliosideGM_{3}(NH_{4}^{+}salt)$	1163 + NH ₃	98+%
1551	N-Hexadecanoyl-D ₉ (13,13,14,14,15,15,16,16,16)-ceramide trihexoside	1033	98+%

Available D₃-Labeled Glycosphingolipids

Catalog No.	Product Name	Formula Weight	Purity
2050	N -omega- CD_3 -Octadecanoyl monosialoganglioside GM_1 (NH_4^+ salt)	1550 + NH ₃	98+%
2051	N -omega- CD_3 -Octadecanoyl monosialoganglioside GM_2 (NH_4^+ salt)	1388 + NH ₃	98+%
2052	N -omega- CD_3 -Octadecanoyl monosialoganglioside GM_3 (NH_4^+ salt)	1185 + NH ₃	98+%
2054	N -omega- CD_3 -Octadecanoyl disialoganglioside GD_3 (NH_4 + salt)	1476 + 2NH ₃	98+%
1537	N-omega-CD ₃ -Octadecanoyl-ceramide trihexoside	1055	98+%

If you cannot find a particular deuterated ganglioside in our catalog, please contact us for a custom synthesis estimate at rdcustomsynthesis@matreya.com

MS Quantification of GM₃ Deficiency

The enzyme ST3GAL5 controls the sialylation of lactosylceramide to produce GM₃, the important precursor for downstream a- and b-series glycosphingolipids (GSLs), including all major, complex gangliosides in neural tissue. Damaging mutations of *ST3GAL5* have been linked to systemic ganglioside deficiency in old order Amish, African -American, French, and Korean populations. In humans, glycosphingolipid deficiency contributes to neonatal hearing loss, stagnant brain growth, epileptic encephalopathy, and cortical visual impairment.¹⁻⁵

A research team consisting of Aoki, Heaps, Strauss, and Tiemeyer developed an elegant technique for mass spectrometric quantification of plasma GSL in human GM_3 ganglioside deficiency from Amish community members with biallelic mutations of *ST3GAL5* (c.694C > T) as well as heterozygous siblings and wild-type controls.⁶ With this method, they identified in *ST3GAL5* (c.694C > T) homozygotes a complete absence of GM_3 and GD_3 and marked accumulation of lactosylceramide with a limited shift in ceramide composition toward higher mass species with longer chain length and alternative saturation. Such structural changes likely alter membrane fluidity and lipid-protein interactions.

We at Matreya produce quality GM₃ that can be used for this quantitation and have a complete line of gangliosides and several mass spectrometry standards for disease biomarkers.

Related Products

Catalog No.	Product Name	Size	Purity
1503	Monosialoganglioside $GM_{_3}$ (NH $_4^+$ salt)	1 mg	98+%
1504	Disialoganglioside GD ₃ (NH ₄ ⁺ salt)	5 mg	98+%
1504-25	Disialoganglioside GD ₃ (NH ₄ ⁺ salt)	25 mg	98+%
2052	$N\text{-}omega\text{-}CD_{3}\text{-}Octade can oyl monosial og anglioside GM_{3} (NH_{4}^{+} salt)$	250 µg	98+%

View Matreya's full list of GM_3 analogs and other ganglioside standards at www.matreya.com

References

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- 5. Wang, H., Bright, A., Xin, B., et al. Cutaneous dyspigmentation in patients with ganglioside GM3 synthase deficiency. Am. J. Med. Genet. A 161A(4), 875-879 (2013).
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Expansion of Our Ganglioside Line

Matreya is a dedicated company in the field of glycolipid chemistry for the past 25 years. Our gangliosides are well known throughout the world. Our products are used in academic, clinical, and industrial laboratories. We feel privileged to continue developing new products to support ganglioside research. In this edition of our newsletter, we are proud to introduce gangliosides from the brains of ovine and porcine in addition to our source of regular bovine brain.



New Ganglioside Standards

Catalog No.	Product Name	Size	Purity
1544	Monosialoganglioside $GM_1 (NH_4^+ salt)$, ovine	5 mg	98+%
1544-50	Monosialoganglioside $GM_1 (NH_4^* salt)$, ovine	50 mg	98+%
1545	Monosialoganglioside $GM_1 (NH_4^+ salt)$, porcine	5 mg	98+%
1545-50	Monosialoganglioside $GM_{_1}(NH_{_4}^{+} salt)$, porcine	50 mg	98+%
1546	Disialoganglioside GD_{1a} (NH $_4^+$ salt), porcine	5 mg	98+%
1547	Disialoganglioside $GD_{_{1b}}$ (NH $_{_4}$ * salt), porcine	1 mg	98+%
1549	Tetrasialoganglioside GQ_{1b} (NH $_4^+$ salt), porcine	100 µg	98+%
1549-001	Tetrasialoganglioside $GQ_{_{1b}}$ (NH $_{_{4}}$ * salt), porcine	1 mg	98+%
1516-001	Tetrasialoganglioside ${\rm GQ}_{_{1b}}$ (NH $_{_{4}}^{_{+}}$ salt), bovine – new size and reduced price!	1 mg	98+%
1548	Trisialoganglioside GT_{1b} (NH $_4^*$ salt), porcine	5 mg	98+%

DIVERSE APPLICATIONS OF MATREYA'S GANGLIOSIDES

To effectively study the effects and pathologies of the highly versatile group of gangliosides, it is important to have an arsenal of suitable and well-defined standards. In response to requests from numerous researchers, Matreya's chemists have produced ganglioside standards for the specific research that is currently underway. With the use of natural and stable isotope-labeled ganglioside standards, researchers can probe the mechanisms of ganglioside functions and metabolism.

For example, Matreya's standards can be used to study...

- \cdot GD₂ and GD₃ expression in cancers where it plays a role in tumor cell attachment to ECM.
- Mutations in the *B4galnt1* gene involved in GM₂, GD₂, and GA₂ biosynthesis.
- · Anti-GD₂ antibody activity against neuroblastoma.
- Neuroprotective GM, and pro-apoptotic GD, involvement in neurodegenerative diseases.
- \cdot GM, and GT, promotion of neuronal differentiation and dendrite generation.
- · GM₁, GD_{1a}, and GT_{1b} inhibition of EGFR, FGR, HGF, and PDGFR signaling in cancer cell membranes.
- \cdot GT_{1b} as a receptor for various toxins, which recognize its oligosaccharide structure.
- \cdot GD $_{\rm 1b}$, GT $_{\rm 1b}$, and GQ $_{\rm 1b}$ inhibition of adenylate cyclase activity to enhance Th1 cytokine production.

View Matreya's full list of ganglioside standards at www.matreya.com